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NEW USSR WORK ON NERVE IMPULSE MEDIATORS, CURARIFORM DRUGS, AND SPASMOLYTICS IN CONNECTION WITH THE THERAPY OF HYPERTENSION

[Comment: The work done in the USSR on hypertension is noteworthy by reason of the emphasis which is placed on the action of nerve impulse mediators and of drugs which block and counteract the action of these mediators. Furthermore, efforts are being made to study the underlying relationships from the standpoint of reflex responses to hypoxia and related effects produced by toxic agents. Under the circumstances, a considerable amount of material which has a bearing on the action of cholinesterase inhibitors and of other toxic agents is being uncovered and published. As far as the work done in this field by S. V. Anichkov's group is concerned, it is often difficult to tell whether the research is on hypertension from the toxicological standpoint, or on toxicology in general with the view of applying some of the results, if that is possible, in the therapy of hypertension. This is presumably due to the fact that some members of Anichkov's group who participate in pharmacological research on drugs for the therapy on hypertension are interested primarily in occupational diseases produced by poisons and toxicological problems in general. In an investigation conducted by the Leningrad State Scientific Research Institute of Labor Hygiene and Occupational Diseases, an attempt has actually been made to establish whether or not there is a correlation between the incidence of hypertension and exposure to certain industrial poisons (V. A. Shtriter, "Concerning the Level of Blood Pressure in Different Occupational Groups," Terapevticheskiy Arkhiv, Vol 26, No 2, Moscow, 1954, pp 50-55). While no correlation was found between hypertension and exposure to benzene, aromatic nitrocompounds, or carbon disulfide, it was established that workers who have been exposed to the action of lead develop a low blood pressure and that workers exposed to the action of mercury have a tendency to develop high blood pressure.

The high incidence of hypertension in the USSR (particularly in Leningrad) is ascribed in USSR publications to the nervous strain imposed by conditions that were prevalent during World War II. The Western approach to the etiology and therapy of hypertension has been severely criticized in the USSR on the ground

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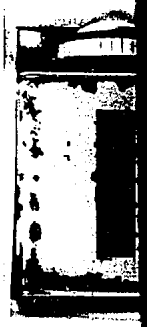


that Western medical men (particularly in the US, where 25% of the population are supposed to be suffering from hypertension) disregard the social aspects of the etiology of the disease, do not pay sufficient attention to the role of the central nervous system in its pathogenesis, and concentrate on eliminating the emotional elements of personal conflict by psychotherapeutic treatment, i.e., psychoanalysis (K. N. Zamyslova, Z. Z. Dorofeyeva, "A Critical Review of Foreign Theories of the Pathogenesis of Hypertension," Vestnik Akademii Meditsinskikh Nauk SSSR, No 4, Moscow 1953, pp 39-51).

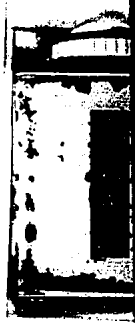
Notwithstanding this criticism, one may conclude on the basis of scientific data published in the USSR that there is substantial agreement with Western views as far as the role played by nervous strain in producing hypertension is concerned. It is true that there are differences in the interpretation of the pathogenesis of the disease and in methods of symptomatic treatment. However, as far as the general approach to the therapy of hypertension is concerned, the difference seems to be this: Western physicians try to eliminate the cause of the conflict, while proponents of Soviet official medicine tend to disregard the causes of the emotional strain (i.e., the social aspects of the etiology of the disease) and instead recommend that the higher nervous activity of the patients be influenced by treatment with drugs.

Numbers in parentheses refer to appended sources.]

The Action of Drugs in Hypertension

Therapy by means of pharmocological agents must consist in the application of substances which bring the activity of the cerebral cortex back to normal. Therapy by means of protective inhibition (sleep therapy) is based on this principle. Among modern hypnotics the derivatives of barbituric acid, i.e., amytal (barbamyl), nembutal, malyl [diallylbarbituric acid], hexenal [methylcyclohexenyl-barbituric acid], and pentothal are being applied most extensively. In order to assure that a condition which is close to normal sleep is induced, one must maintain a relatively low concentration of the hypnotic in the body. To achieve this purpose, barbiturates which exhibit a medium duration of action, namely amytal and nembutal, have been found most suitable. Cholinolytic and adrenolytic substances, i.e., TEA (tetraethyl-ammonium salts) and sympatholytin, are of great importance as therapeutic agents. The blocking of vasoconstrictive impulses may be carried out at two points, i.e., at the sympathetic ganglia, where acetylcholine functions as the mediator, and in the region where the postganglionic sympathetic fibers terminate and where adrenalin and noradrenalin serve as transmitters of impulses. Neither TEA nor symptholytin were found suitable for the treatment of hypertension. Sympatholytin, which is the most effective of all drugs of this type and which proved very valuable for physiological experiments, is not devoid of toxic properties. It shares this characteristic with other sympathicolytic drugs, which have been proposed earlier. TEA on thorough investigation also was found unsuitable for effecting a block of the sympathetic ganglia. It is true that TEA is not very toxic. However, in being resorbed, this drug blocks parasympathetic ganglia earlier than the sympathetic ones.

To block ganglia one may use the diphenylacetic ester of diethylaminoethanol (diphacyl), which at present is the best agent for that purpose, particularly as far as blocking of the sympathetic chain in regional angiospasms is concerned. Diphacyl is also effective in the therapy of ischialgias and gastrointestinal ulcers. However, in the therapy of hypertension, diphacyl did not yield encouraging results, possibly because this method and the way of applying it in hypertension have not been investigated adequately as yet. Alleviation of vascular spasms and weakening of the effect of vasoconstrictive impulses may be achieved by using substances which have a myotropic effect, i.e., act on the constrictive elements of the vascular system. This effect is produced by representatives of the nitroglycerine and nitrates group, salts of theobromine and theophylline, and plant alkaloids of the papaverine type. The original synthetic Soviet drug dibazol and



phenatin [beta-phenylisopropylamide of nicotinic acid] are drugs of the papaverine type. To reduce the current of impulses which maintain a high tonus of blood vessels, one must exert action on the chemoreceptors and on the centers connected with the chemoreceptors. This can be achieved by administering novacain intravenously. As a result of the administration of this drug the elimination of sympthin at the endings of the vascular motor nerves is reduced. At the present time it is possible to modify the sensitivity of chemoreceptors by acting on their tissue metabolism. Specifically, it has been established that administration of glucose raises the reactivity of the carotid chemoreceptors and lowers the excitability of the centers connected with them. This action of glucose makes possible a new interpretation of the effect exerted by it in hypertension. Not only the interoreceptors, but also the exteroreceptors are of importance in effects exerted by drugs that are of value in the treatment of hypertension.

As far as the therapy of hypertension with drugs that affect exteroreceptors is concerned, it is up to pharmacologists not only to investigate substances which have a selective effect on skin receptors, but also drugs which lower the sensitivity and inhibit it temporarily. Local anesthetics are substances that exert this type of action. This applies particularly to novocain, which is used to establish the so-called regional skin blocks. The powerful effects exerted on the trophism and on the blood circulation by reflexes which originate at the skin form the basis of the action of such remedies as mustard plasters, leeches, mineral water baths, etc., which have been used in the therapy of circulation disturbances for a long time. However, the application of therapeutic methods of this type is not based on physiological knowledge, but is purely empirical. What should be studied is not only the problem of the selection of suitable anesthetics, but also the question of choosing the appropriate zone where a regional block should be applied. It is necessary to take into consideration that the drug in addition to exerting a local action must also have an effect by virtue of its resorption.(1)

After the mechanism of the action of some substances which have a hypotensive effect (diisopropyl-putrescine, salsoline, barbamyl, etc.) had been investigated on animals, the therapeutic effect exerted by these substances was checked in clinical practice. On administration of diisopropyl-putrescine, the blood pressure of patients drops because this substance blocks the transmission of impulses through ganglia of the vegetative nervous system. Intravenous administration of salsoline together with a 0.25% solution of novocain brings about a lasting drop in arterial pressure, because impulses originating at interoreceptors do not reach the central nervous system. Barbamyl given internally and simultaneous intravenous administration of a 10% solution of calcium chloride were found to have the best effect in the treatment of hypertension.(2)

The principal therapeutic problem in hypertension is restoration of the normal interrelationship between processes of excitation and inhibition in the cerebral cortex and the lower nervous centers. In cerebral forms of hypertension on a good effect was obtained by injecting magnesium sulfate intravenously and by administering thiocyanates. In addition to ordinary spasmolytics (nitroglycerine, papaverine, salsoline, myol[a protein-free extract of striated muscles of cattle which has a vasodilative effect], etc., thiplen [the hydrochloride of the beta-diethylamincethyl ester of thiodiphenylacetic acid] in combination with promedol [propionic acid ester of 1,2,5-trimethyl-4phenyl-4-piperidol] was used for the first time and found to be effective.(3)

The Pathogenesis of Hypertension

The assumption that adrenalin exerts the main effect as an autogenous mediator in hypertension is open to criticism. Investigations which have been carried out indicate that noradrenalin (artherenol) rather than adrenalin functions as the mediator which produces hypertension. It has been established that noradrenalin

raises the arterial pressure to a much greater extent than adrenalin administered in the same doses.(4)

As distinguished from adrenalin, noradrenalin produces a spasmodic condition of arterioles throughout the body. For that reason, its action in raising the blood pressure is much stronger than that of adrenalin.

Investigation of the blood of patients suffering from hypertension showed that there are shifts which indicate a reduction in the intensity of oxidative processes and are expressed in an accumulation of amino acids, polypeptides, and ketones. To establish the reasons for the reduction in the relative intensity of oxidation processes, investigations were conducted on rabbits which had hypertension. The respiration of different organs was studied after hypertension had been induced by tieing up both depressors of the aorta and denervating the carotid sinuses. A clear dependence between the reduction of the level of respiration and the time at which hypertension had been induced could not be established. The consumption of oxygen by sections of the kidneys, the liver, and the cerebral cortex was determined in animals which had renal hypertension of varying duration. Investigation of ischemic tissues demonstrated that even after the disappearance of ischemia there is an excess of oxygen; the tissues are injured and do not breathe fully. The same processes take place in vitro: first the tissue does not receive enough oxygen, while later, because of injury and prior oxygen starvation, it cannot use the oxygen which it receives.(5)

It was possible to induce hypertension in rabbits by subjecting them to a trauma: a bright flame was made to appear in front of them while beakers filled with hot water were placed simultaneously on their backs, which had been shaved prior to that. This method was modified later by adding a loud noise. The experiments in question indicate that hypertension can be produced by acting on the cerebral cortex. In experiments carried out by R. Y. Spivak, humoral hypertension was produced in rabbits by injecting them intravenously with the blood serum of patients suffering from hypertension. The hypertensive agents contained in the serum acted on the central nervous system by the way of the interoreceptors. The central nervous system in turn affected the cardiovascular system, causing hypertension.(6)

In the functional phase of hypertension there is an imbalance of the vegetative nervous system. The terminal phase and the rapidly progressing forms of the disease are marked by an inhibition of mental activity and a predominance of the functioning of the parasympathetic division of the vegetative nervous system.(8)

Disturbances of Tissue Respiration in Hypertension

Biochemical investigations carried out by workers at the Georgian Institute of Clinical and Experimental Cardiology established that in hypertension a direct effect is exerted on the heart and on the walls of blood vessels by adrenalin and compounds of thyramine, hydroxythyramine, and noradrenalin. The functional condition of the central nervous system exerts an influence on the formation of these substances and on the intensity of their action. It has been established that tissue hypoxia, acidosis, and accumulation in the body of products of incomplete oxidation play a significant role in experimental hypertension. An ischemic condition of the kidneys, which results in oxygen starvation of the tissues, contributes to the liberation of a pressor substance (renol) from an inactive compound. Clinical observations on patients have confirmed that hypoxic shifts and disturbances of metabolism occur in hypertension.(9)

Oxygen Therapy of Hypertension

Therapy with oxygen (use of an oxygen tent) in combination with the administration of drugs was found beneficial in the second stage of hypertension. In the third stage of the disease application of oxygen resulted only in a temporary improvement.(10) If the oxygen therapy is supplemented by the administration of glucose or of glucose and insulin, the consumption of oxygen is increased.(11)

SOURCES

1. S. V. Anichkov, "The Problem of the Drug Therapy of Hypertension and of Angiospasms in the Light of I. P. Pavlov's Teaching," Vestnik Akademii Meditsinskikh Nauk SSSR, No 3, Moscow 1953, pp 20-27

2. Moscow, Sovetskoye Meditsinskoye Referativnoye Obozreniye, No 19, 1955, p 60. Abstract of article by S. S. Gvishiani, "Concerning the Mechanism of the Action of Some Hypotensively Acting Substances in Hypertension," which appeared in Vrachebnoye Delo, No 1, 1954, pp 19-22

3. V. I. Kristman, "Therapy of Hypertension Patients in a State of Crisis," Sovetskaya Meditsina, Vol 17, No 10, Moscow 1953, pp 7-10

4. Sovetskoye Meditsinskoye Referativnoye Obozreniye, No 19, 1955, p 70. Abstract of article by O. A. Stepan, "The Second Hormone of the Medullar Part of the Suprarenals (Noradrenalin) and Its Participation in the Genesis of Hypertension," which appeared in Vrachebnoye Delo, No 1, 1954, pp 9-14

5. Ibid., p 63 Abstract of article by N. K. Kvirikadze, "Concerning the Investigation of Tissue Redox Processes in Various Types of Experimental Hypertension," which appeared in Vrachebnoye Delo, No 1, 1954, pp 25-30

6. Ibid., pp 63-64. Abstract of article by V. M. Kogan-Yasnyy, "Some Clinicoexperimental Data Pertaining to Corticovisceral Factors in Hypertension and Gastrointestinal Ulcers," which appeared in Problemy Kortiko-Vistseral'noy Patologii (Problems of Corticovisceral Pathology), Moscow/Leningrad, 1952, pp 21-37

7. Ibid., p 65. Abstract of article by A. L. Landa, "The State of Excitability of Higher Nervous Centers in Hypertension," which appeared in Problemy Kortiko-Vistseral'noy Patologii, pp 202-205

8. Ibid., p 65. Abstract of artcle by R. Z. Lur'ye, "The Correlation Between the Pathology of the Nervous System and That of the Cardiovascular System," which appeared in Trudy Vtoroy Rasshirennoy Nanchnoy Sessii Instituta Klinicheskoy Eksperimental'noy Kardiologii, Posvyashchennoy Probleme Gipertoincheskoy Bolezni (Work of the Second Expanded Scientific Session of Clinical and Experimental Cardiology Devoted to the Problem of Hypertension), Tbilisi, 1953, pp 151-158

9. Ibid., pp 67-68. Abstract of article by F. Ya Primak, "Problems of Hypertension Discussed at the Scientific Session of the Institute of Cardiology Academy of Sciences Georgian SSR, Held Together With the Institute of Physiology, Academy of Sciences Ukrainian SSR," which appeared in Vrachebnoye Delo, No 10, 1953, pp 951-954

10. Ibid., p 67. Abstract of article by M. Z. Pogorelova and K. D. Kozlenko, "Experience in the Application of Oxygen Therapy in Hypertension," which

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appeared in Vrachebnoye Delo, No 1, 1954, pp 71-72

11. Sovetskoye Meditsinskoye Referativnoye Obozreniye, No 19, 1955, p 72. Abstract of article by D. F. Chebotarev and M. Ye. Malyarevskaya, "The Effects of Glucose and of Insulin on the Gas Metabolism of Patients Suffering From Hypertension Who Are Being Subjected to Oxygen Therapy," which appeared in Vrachebnoye Delo, No 1, 1954, pp 23-26

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